

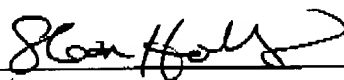
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Attorney's Docket No. 3477-89

PATENT

In re: Application of Egan et al.
Serial No.: 09/674,237
Filed: July 24, 2001
For: *ESE GENES AND PROTEINS*

Group: 1646

Submission of:

1. Claims as filed

Pending Claims – Egan et al.**Appl'n Serial No. 09/674,237****Your Ref. 3206-192/PAR:al; Our File No. 3477-89**

1. An isolated nucleic acid comprising a nucleotide sequence encoding a mammalian Ese1 protein or a splice variant thereof.
2. The nucleic acid of claim 1, wherein said nucleotide sequence encodes a murine Ese1 protein or a splice variant thereof.
3. The nucleic acid of claim 1, wherein said nucleotide sequence encodes a human Ese1 protein or a splice variant thereof.
4. The nucleic acid sequence of claim 1, wherein said nucleic acid comprises a nucleotide sequence selected from the group consisting of a genomic sequence, a cDNA sequence, a polydeoxyribonucleic acid nucleotide sequence, a polyribonucleic acid nucleotide sequence, an allelic variant or homologue thereof.
5. The nucleic acid of claim 1 encoding a protein comprising the amino acid sequence of Sequence ID No. 3 or Sequence ID No. 24.
6. The nucleic acid of claim 1 comprising the sequence of Sequence ID No. 1, Sequence ID No. 2, Sequence ID No. 22 or Sequence ID No. 23.
7. An isolated nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides selected from the group consisting of Sequence ID No. 1, Sequence ID No. 2, Sequence ID No. 22, Sequence ID No. 23 and a sequence complementary to any of these sequences.
8. The nucleic acid of claim 7, wherein said sequence is used as a probe or a primer.

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9. (Amended) A recombinant vector comprising the isolated nucleic acid of claim 1
10. A host cell comprising the recombinant vector of claim 9.
11. A substantially pure mammalian Ese1 or Ese1L protein.
12. A substantially pure murine Ese1 or Ese1L protein.
13. A substantially pure human Ese1 or Ese1L protein.
14. The protein of claim 11 wherein the protein comprises an Ese1 protein comprising the amino acid sequence of Sequence ID No. 3 or the Ese1L protein comprising the amino acid sequence of Sequence ID No. 24.
15. A substantially pure polypeptide comprising an amino acid sequence of at least 5 consecutive amino acid residues of Sequence ID No. 3 or Sequence ID No. 24.
16. A substantially pure polypeptide comprising at least one functional domain of a mammalian Ese1 protein or a mammalian Ese1L protein.
17. A substantially pure polypeptide comprising an antigenic determinant of a mammalian Ese1 protein or a mammalian Ese1L protein.
18. An antibody which binds specifically to a polypeptide of claim 16.

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19. (Amended) A process for recombinantly producing murine Ese1 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 2[, 3 or 4] under conditions whereby the Ese1 protein is expressed and isolating the Ese1 protein therefrom.
20. An isolated nucleic acid comprising a nucleotide sequence encoding a mammalian Ese2 protein or a splice variant thereof.
21. The nucleic acid of claim 20, wherein said nucleotide sequence encodes a murine Ese2 protein or a splice variant thereof.
22. The nucleic acid of claim 20, wherein said nucleotide sequence encodes a human Ese2 protein or a splice variant thereof.
23. The nucleic acid sequence of claim 20, wherein said nucleic acid comprises a nucleotide sequence selected from the group consisting of a genomic sequence, a cDNA sequence, a polydeoxyribonucleic acid nucleotide sequence, a polyribonucleic acid nucleotide sequence, an allelic variant or homologue thereof.
24. The nucleic acid of claim 20 encoding a protein comprising the amino acid sequence of Sequence ID No. 6 or Sequence ID No. 27.
25. The nucleic acid of claim 20 comprising the sequence of Sequence ID No. 4, Sequence ID No. 5, Sequence ID No. 25 or Sequence ID No. 26.
26. An isolated nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides selected from the group consisting of Sequence ID

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No. 4, Sequence ID No. 5, Sequence ID No. 25, Sequence ID No. 26 and a sequence complementary to any of these sequences.

27. The nucleic acid of claim 26, wherein said sequence is used as a probe or a primer.
28. (Amended) A recombinant vector comprising the isolated nucleic acid of claim 20
29. A host cell comprising the recombinant vector of claim 28.
30. A substantially pure mammalian Ese2 or Ese2L protein.
31. A substantially pure murine Ese2 or Ese2L protein.
32. A substantially pure human Ese2 or Ese2L protein.
33. The protein of claim 32 wherein the protein comprises an Ese2 protein comprising the amino acid sequence of Sequence ID No. 6 or the Ese2L protein comprising the amino acid sequence of Sequence ID No. 27.
34. A substantially pure polypeptide comprising an amino acid sequence of at least 5 consecutive amino acid residues of Sequence ID No. 6 or Sequence ID No. 27.
35. A substantially pure polypeptide comprising at least one functional domain of a mammalian Ese2 protein or a mammalian Ese2L protein.

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36. A substantially pure polypeptide comprising an antigenic determinant of a mammalian Ese2 protein or a mammalian Ese2L protein.
37. An antibody which binds specifically to a polypeptide of claim 36.
38. (Amended) A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 20[, 21 or 22] under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.
39. A pharmaceutical composition for the treatment of mammalian disorders which involve abnormal endocytosis leading to altered cellular functioning, said composition comprising an active ingredient selected from the group consisting of;
 - a) an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2, Ese2L,
 - b) a fragment or mimetic thereof or a non-functional mutant protein, fragment or mimetic thereof of the proteins of a); and
 - c) a pharmaceutically acceptable carrier.
40. A method of screening a candidate compound for efficacy in treating a disorder characterized by an abnormality in the endocytotic pathway, wherein said pathway involves an interaction between an Ese1, Ese1L, Ese2 or Ese2L protein and a binding partner of any one of these proteins, comprising screening said candidate compound for its ability to disrupt or promote said interaction as an indication of its efficacy.

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41. A method for preventing or treating a disorder in a mammal characterized by an abnormality in the endocytotic pathway, wherein said pathway involves an interaction between an Ese1, Ese1L, Ese2 or Ese2L protein and a binding partner of any one of these proteins, comprising the step of disrupting or promoting said interaction *in vivo*.
42. (Amended) The method of claim 40[or 41], wherein said disorder is selected from the group consisting of cancer, abnormal cell division, abnormal cell migration, viral infection, abnormal receptor signalling, abnormal tissue development and abnormal synaptic transmission disorders.
43. A method for screening a candidate compound for effectiveness as an antagonist of an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L, said method comprising:
- (a) providing an assay method for determining the endocytotic regulatory capacity of a selected Ese protein; and
 - (b) determining the endocytotic regulatory capacity of the selected Ese protein in the presence or absence of the candidate compound, wherein a reduced level of endocytotic regulatory capacity in the presence of the candidate compound indicates effectiveness of the compound as an antagonist.
44. A method for treating in a mammal a disorder associated with an undesired level of endocytotic activity of an Ese protein selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L, said method comprising administering to the mammal an effective amount of a substance selected from the group consisting of:

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- (a) an Ese protein antagonist;
- (b) an antibody which binds specifically to an Ese protein;
- (c) an antisense strand comprising a nucleic acid sequence complementary to a sequence or fragment of the sequence represented by Sequence ID Nos. 1, 2, 4, 5, 22, 23, 25 and 26 and capable of hybridizing to the nucleic acid sequence encoding an Ese protein;
- (d) an agent which down regulates the expression of an Ese gene encoding for an Ese protein;
- (e) an antagonist of an Ese protein binding partner; and
- (f) an Ese agonist.
45. A method for suppressing in a mammal, abnormal proliferation of a cell capable of being stimulated to proliferate by a growth factor receptor, the method comprising administering to the mammal an effective amount of a Ese protein antagonist, an Ese agonist or an antibody which binds specifically to an Ese protein, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.
46. A method for preventing viral infection in a mammal, said method comprising administering to the mammal an effective amount of an Ese protein antagonist, an Ese agonist or an antibody which binds specifically to an Ese protein or an Ese mutant protein not capable of regulating endocytosis, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.
47. A method for promoting endocytosis in selected cells in a mammal in need of such treatment, said method comprising administering to the mammal an effective amount of an Ese protein or an active analogue, mimic or

Antagonist + Ab → anti Ese.
Agonist - Ab
Antagonist = anti
Agonist = anti

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fragment thereof, wherein the Ese protein is selected from the group consisting of Ese1, Ese1L, Ese2 and Ese2L.

48. A method for blocking clathrin-mediated endocytosis in cultured cells or in selected cells in a mammal in need of such treatment, said method comprising overexpressing Ese1 protein or an active analogue, mimic or fragment thereof in said cells.
49. A method for regulating endocytosis in cultured cells or in selected cells in a mammal in need of such treatment, said method comprising providing an Ese1-Esp15 complex and further binding dynamin to said complex to regulate components of the endocytic pathway.
50. A recombinant vector comprising the isolated nucleic acid of claim 7.
51. A host cell comprising the recombinant vector of claim 50.
52. A process for recombinantly producing murine Ese1 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 3 under conditions whereby the Ese1 protein is expressed and isolating the Ese1 protein therefrom.
53. A process for recombinantly producing murine Ese1 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 4 under conditions whereby the Ese1 protein is expressed and isolating the Ese1 protein therefrom.
54. A recombinant vector comprising the isolated nucleic acid of claim 26.

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55. A host cell comprising the recombinant vector of claim 54.
56. A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 21 under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.
57. A process for recombinantly producing murine Ese2 protein comprising culturing a host cell comprising a recombinant vector comprising the nucleic acid of claim 22 under conditions whereby the Ese2 protein is expressed and isolating the Ese2 protein therefrom.
58. The method of claim 41, wherein said disorder is selected from the group consisting of cancer, abnormal cell division, abnormal cell migration, viral infection, abnormal receptor signalling, abnormal tissue development and abnormal synaptic transmission disorders.